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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,071	02/13/2002	David Bar-Or	4172-3-2	8825

22442 7590 04/04/2007

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EXAMINER	
DESAI, ANAND U	
ART UNIT	**PAPER NUMBER**
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/076,071	BAR-OR ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *531-542,544-548,550-555 and 558-580* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *531-542,544-548,550-555 and 558-580* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 23, 2007 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawal of Rejections

3. The rejection of claims 559-562, and 567 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn based on the amendment to the claims.

4. The rejection of claims 531-542, 544-548, and 550-576 under 35 U.S.C. 102(b) as being anticipated by Hagiwara, D. et al. (JP 62-116565, IDS filed June 18, 2002, document 87) is withdrawn based on the art, particularly Jones et al., describing the requirement of angiogenesis during the healing of ulcers.

5. The rejection of claims 531-542, 544-548, and 550-576 under 35 U.S.C. 102(b) as anticipated by Heavner et al. (WO 95/26744, IDS filed 2/17/2006, document AC) or, in the

alternative, under 35 U.S.C. 103(a) as obvious over Heavner et al. (WO 95/26744, IDS filed 2/17/2006, document AC) in view of Shimazawa et al. (Biol. Pharm. Bull. 22(2): 224-226 (1999)) is withdrawn because none of the peptides of Heavner et al. are encompassed by the formula of peptides recited.

Maintenance of Rejections

Claim Rejections - 35 USC § 112, Enablement

6. Claims 531-542, 544-548, 550-555, and 558-580 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an angiogenic disease or condition by inhibiting angiogenesis using metal-binding peptides as disclosed in the examples and the declaration filed April 20, 2006, does not reasonably provide enablement for a method of treating an angiogenic disease or condition with a metal-binding peptide encompassed by the formula, P_1-P_2; P_1 is Xaa_1 Xaa_2 His or Xaa_1 Xaa_2 His Xaa_3, the P_1 portion of the peptide is linear, P_2 is $(Xaa_4)_n$, where n is 0-10, and Xaa_1, Xaa_2, Xaa_3, and Xaa_4 are amino acids disclosed in claim 531. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was explained in the office action mailed September 30, 2005 and further discussed in the office action mailed July 25, 2006.

Response to Remarks

7. The declaration under 37 CFR 1.132 filed April 20, 2006 is insufficient to overcome the rejection of claims 531-542, 544-548, 550-555, and 558-580 based upon 35 U.S.C. § 112, first

paragraph, scope of enablement as set forth in the previous Office action because: the showing is not commensurate in scope of the claims.

The claims are drawn to a method of treating an angiogenic disease or condition in an animal comprising administering to the animal an amount of a metal-binding peptide which does not have a metal bound to it or a physiologically-acceptable salt of the peptide, the amount of the peptide or salt which is administered to the animal being effective to inhibit angiogenesis, the sequence of the peptide being P_1-P_2; P_1 is Xaa_1 Xaa_2 His or Xaa_1 Xaa_2 His Xaa_3, the P_1 portion of the peptide is linear, P_2 is $(Xaa_4)_n$, where n is 0-10, and Xaa_1, Xaa_2, Xaa_3, and Xaa_4 are amino acids disclosed in the claims.

Applicants Remarks dated September 7, 2005 state there was not sufficient predictability in the art of inhibiting angiogenesis using metal chelating agents at the time of the filing of the application (see also scope of enablement, section 3 of Office action mailed September 30, 2005). In reference to the newly presented claims (577-580) encompassing a glycine amino acid residue at position Xaa_2 (see 3rd indented paragraph in Remarks/Arguments filed January 23, 2007), the prior enablement rejection describes the unpredictable nature of copper binding peptides with a glycine at position 2. The Lane, T et al. reference describes a peptide sequence, L-Lys-L-Gly-L-His-L-Lys, which stimulates angiogenesis (see scope of enablement, section 3 of Office action mailed September 30, 2005). Accordingly, there is unpredictability for metal-binding peptides ability to inhibit angiogenesis.

The declaration further describes assays that have copper bound with the metal-binding peptides to describe the inhibition of angiogenesis, whereas the claims are drawn to a metal-

binding peptide that does not have a metal ion bound. Figures A through LL have peptides complexed with copper ions.

The HUVEC proliferation assay describes peptides, Tyr-Lys-His, Ser-Ser-His, D-Phe-Gly-His, and Asp-Ala-His-Arg-Arg-Arg-Arg-Arg-Arg that do not inhibit proliferation of endothelial cells, and do not inhibit angiogenesis.

Therefore, there is unpredictability for metal-binding peptides ability to inhibit angiogenesis. There is no way to predict whether all of the metal-binding peptides encompassed by the formulas in the claims will treat an angiogenic disease or condition by inhibiting angiogenesis. There is insufficient guidance and a large quantity of experimentation to make and use the peptides of the invention within the full scope of the claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 531-539, 544, 559-567, 569-578, and 580 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harford and Sarkar (Acc. Chem. Res. 30: 123-130 (1997); previously cited) in view of Hu, G. (Journal of Cellular Biochemistry 69: 326-335 (1998)).

Harford and Sarkar disclose the amino terminal copper and nickel-binding motif found in proteins (see Introduction, pp.123). Harford and Sarkar disclose the binding of copper and

nickel to the amino acid sequence Asp-Ala-His, which is a peptide being claimed by the formula in claims 531 and 577 (see Figure 3-5, pp. 125). Harford and Sarkar describe the importance of the Histidine residue being in the 3rd position of an amino acid sequence to bind a copper ion (see section on Design of the ATCUN Motif, pp. 126). Harford and Sarkar further disclose the synthetic design of a metal binding site onto a protein, to produce a hybrid protein that is currently being claimed (see Protein Design Utilizing the ATCUN Motif pp. 128, and Conclusion, pp. 130, see current application, claim 531, 542, and 550 in particular).

Hu discloses the effects of copper on angiogenesis. Hu states copper is recognized to be angiogenic. Copper ions induce neovascularization in the rabbit cornea pocket assay (see page 326, Introduction, beginning of 2nd indented paragraph). Copper is a potent inducer of cell proliferation for human endothelial cells (see page 332, 1st sentence of Discussion section).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to design a metal binding peptide as described in Harford and Sarkar, to chelate copper ions and inhibit angiogenesis as described by Hu, because of the desire to treat various angiogenic diseases or conditions, including neoplasms (current application, claims 531-539, 544, 559-567, 569-578, and 580).

Conclusion

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

March 28, 2007

ROBERT A. WAX
PRIMARY EXAMINER